

FORM PTO-1390 (REV 10/95)	U. S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY'S DOCKET NUMBER HACK 205
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		U.S. APPLICATION NO. (IF KNOWN, SEE 37 CFR <b>10/018045</b>
INTERNATIONAL APPLICATION NO. PCT/AU00/00641	INTERNATIONAL FILING DATE 07 June 2000	PRIORITY DATE CLAIMED 8 June 1999
TITLE OF INVENTION <b>SMALL CYCLIC MIMICS OF BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF)</b>		
APPLICANT(S) FOR DO/EO/US Richard HUGHES et al.		
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:		
<p>1. <input checked="" type="checkbox"/> This is the FIRST submission of items concerning a filing under 35 U.S.C. 371.</p> <p>2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.</p> <p>3. <input checked="" type="checkbox"/> This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(l).</p> <p>4. <input checked="" type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.</p> <p>5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2))</p> <ul style="list-style-type: none"> <li>a. <input checked="" type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau.)</li> <li>b. <input type="checkbox"/> has been transmitted by the International Bureau.</li> <li>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</li> </ul> <p>6. <input type="checkbox"/> A translation of the International Application into English (35 U.S.C. 371(c)(2)).</p> <p>7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))</p> <ul style="list-style-type: none"> <li>a. <input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau).</li> <li>b. <input type="checkbox"/> have been transmitted by the International Bureau.</li> <li>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li> <li>d. <input type="checkbox"/> have not been made and will not be made.</li> </ul> <p>8. <input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).</p> <p>9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</p> <p>10. <input type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</p> <p>Items 11. to 16. below concern document(s) or information included:</p> <p>11. <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</p> <p>12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</p> <p>13. <input checked="" type="checkbox"/> A FIRST preliminary amendment.</p> <ul style="list-style-type: none"> <li><input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment.</li> </ul> <p>14. <input type="checkbox"/> A substitute specification.</p> <p>15. <input type="checkbox"/> A change of power of attorney and/or address letter.</p> <p>16. <input checked="" type="checkbox"/> Other items or information:</p> <ol style="list-style-type: none"> <li>1. PCT/IPEA/409 (International Preliminary Examination Report)</li> <li>2. PCT/IPEA/408 (Written Opinion dated July 17, 2001)</li> <li>3. Response to Written Opinion dated April 5, 2000</li> <li>6. Unexecuted Declaration/Power of Attorney</li> </ol>		

EXPRESS MAIL NO. EL 649538180 US MAILED December 10, 2001

10/018045

JC07 Rec'd PCT/PTO 10 DEC 2001

## BASIC NATIONAL FEE (37 CFR 1.492(A)(1) - (5)):

Search Report has been prepared by the EPO or JPO ..... \$890.00

International preliminary examination fee paid to USPTO (37 CFR 1.482)  
..... \$710.00

No international preliminary examination fee paid to USPTO (37 CFR 1.482)  
but international search fee paid to USPTO (37 CFR 1.445(a)(2)) ... \$740.00

Neither International preliminary examination fee (37 CFR 1.482) nor  
international search fee (37 CFR 1.445(a)(2)) paid to USPTO ..... \$1040.00

International preliminary examination fee paid to USPTO (37 CFR 1.482)  
and all claims satisfied provisions of PCT Article 33(2)-(4) ..... \$100.00

## ENTER APPROPRIATE BASIC FEE AMOUNT =

\$1040.00

Surcharge of \$130.00 for furnishing the oath or declaration later than  20  30 months from the earliest claimed priority date (37 CFR 1.492(e)).

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	46	- 20 =	x \$18/9	\$ 234.00
Independent	1	- 3 =	x \$80/40	\$ --
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			x \$270/135	\$
TOTAL OF ABOVE CALCULATIONS =				\$1404.00

Reduction of ½ for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28).

SUBTOTAL = \$702.00

Processing fee of \$130.00 for furnishing the English translation later than  20  30 months from the earliest claimed priority date (37 CFR 1.492(f)).

+

TOTAL NATIONAL FEE = \$702.00

Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property+

TOTAL FEES ENCLOSED = \$702.00

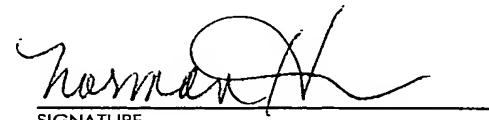
Amount to be: refunded	\$
charged	\$

- a.  A check in the amount of \$ 702.00 to cover the above fees is enclosed.
- b.  Please charge my Deposit Account No. 50-0624 in the amount of \$ to cover the above fees.  
A duplicate copy of this sheet is enclosed.
- c.  The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 50-0624. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

## SEND ALL CORRESPONDENCE TO:

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30,946  
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I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service on the date indicated above and is addressed to: Commissioner of Patents and Trademarks, Washington D.C. 20231

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17 July 2001

Madam

**IN THE MATTER OF International Patent Application No. PCT/AU00/00641  
in the name of THE UNIVERSITY OF MELBOURNE  
Entitled SMALL CYCLIC MIMICS OF BRAIN-DERIVED NEUROTROPHIC  
FACTOR (BDNF)  
Our Ref: SJB:AN:FP12888**

We refer to the first Written Opinion dated 7 March 2001 issued by the International Preliminary Examining Authority in respect of this application.

The applicant notes that there were no novelty or inventive step objections raised against claims 3-23, 26-30, 35, 36, 39, 40, 44, 45, 50 and 51. However, the applicant also notes that novelty and inventive step objections have been taken against claims 1, 2, 24, 25, 31-34, 37, 38, 41-43, 46-49 and 52. In response, the applicant lodges herewith substitute page 72 containing revised claim 1, and the applicant respectfully submits that, in the light of these proposed amendments, all of the claims are novel and inventive over the cited prior art documents.

Specifically, the applicant considers that claim 1 now specifically disclaims brain-derived neurotrophic factor (BDNF) *per se* and other neurotrophic factors such as NGF, NT-3 and N-4/5. Moreover, claim 1 is restricted to compounds that are not derived from NGFNT-3 or NT-4/5 or monocyclic monomeric compounds derived from loop 2 of BDNF. In other words, the cyclic compounds now claimed do not include any compounds disclosed in any of the prior art documents cited in the Written Opinion.

Documents D4 to D6 for example, are directed towards BDNF *per se* or pharmaceutical formulations thereof. None of these documents relate to cyclic compounds of molecular weight less than 3,000 daltons that have the biological activity of BDNF.

Document D1 is a publication of the inventors and relates to monomeric monocyclic peptides derived from loop 2 of BDNF. This publication does not disclose dimers or monomeric monocyclic peptides derived from loop 4 of BDNF. Furthermore, the dimerisation is counter to what would be predicted from alanine scanning as disclosed in D1.

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The Commissioner of Patents

17 July 2001

Document D2 only discloses monomeric monocyclic peptides derived from NGF loops. For example on page 14 it is stated that:

“the antagonistic property of the analogue suggest that for agonistic binding ligand must either engage more than one cite on a given receptor, or possess the ability to induce receptor dimerisation”

In other words this document does not disclose dimers nor does it disclose BDNF sequences. Indeed there is no mention of BDNF. While, this document may disclose cyclic peptides which are capable of binding to BDNF peptides, there are no concrete examples or sequences of BDNF disclosed. Accordingly, in the light of the proposed amendments which specifically disclaims peptides based upon NGF, the present invention is novel and inventive over document D2.

Document D3 does not disclose BDNF. Indeed, document D3 is directed towards novel sequences that are *unrelated* to BDNF, or any other neurotrophin or neurotrophic factor. Document D3 discloses hypocampal cholinergic neutrophic factor (HCNP). While HCNP is isolated from brain, this does not make it BDNF. BDNF is a specific factor that has been identified in the literature previously. Document D3 discloses monomeric peptides although there are some monomeric monocyclic peptides also disclosed.

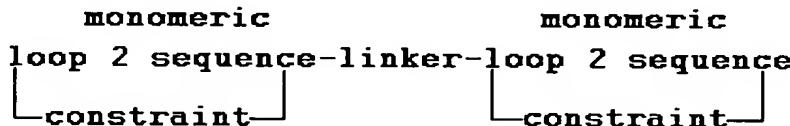
Accordingly, the applicant respectfully submits that none of the prior art cited by the Examiner in any way discloses or teaches towards the presently claimed invention.

Favourable reconsideration is respectfully requested.

Yours faithfully

**CLAIMS:**

- 1). A cyclic compound comprising one or more cyclic moieties, which has a biological activity of brain-derived neurotrophic factor (BDNF), and a molecular weight less than 3,000 daltons with the proviso that the compound is not derived from NGF, NT-3 or NT-4/5 or a monocyclic monomeric compound derived from loop2 of BDNF.
  - 2). A compound according to claim 1, wherein the compound is monocyclic monomeric, bicyclic dimeric, or tricyclic dimeric.
  - 3). A compound according to claim 2, wherein the compound is a bicyclic dimeric compound of general formula (I):

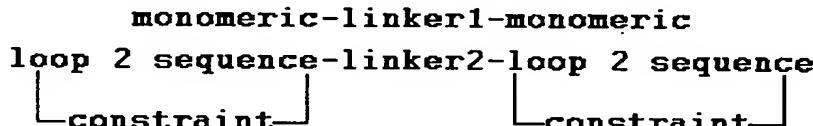


(I).

- 20 4). A compound according to claim 3, wherein the constraint comprises a covalent grouping of atoms.

5). A compound according to claim 4, wherein the constraint and the linker may be the same or different.

25 6). A compound according to claim 2, wherein said compound is a tricyclic dimeric compound of general formula (II):



(II).

- 30 7). A compound according to claim 6, wherein each of  
the constraint, linker 1 and linker 2 may be the same or